Translation

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PCT Application
PCT/JP2002/003239

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AN006PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP02/03239	International filing date (*day/month/year*) 29 March 2002 (29.03.02)	Priority date (*day/month/year*)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 48/00, 31/711, A61P 25/00, 43/00		
Applicant	ANGES MG, INC.	

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 19 August 2002 (19.08.02)	Date of completion of this report 08 April 2003 (08.04.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP02/03239

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 11-20

because:

☒ the said international application, or the said claims Nos. 11-20 relate to the following subject matter which does not require an international preliminary examination *(specify):*

The subject matters of claims 11-20 relate to a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34 (4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 11-20 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

If claim 1 of the present application is considered as a specified invention, a matter common to both claims 1 and 7 is considered to be "letting a decoy reach the brain." However, since "letting a decoy reach the brain" is publicly known as described in the following document, the constitution is not considered to be a novel matter and is not considered to be a feature of the invention either.

Furthermore, the subject matter of claim 7 of the present application is "a composition used for transfecting a gene in the brain through any other route than direct administration to the brain, characterized by containing at least one decoy and a pharmaceutically acceptable carrier." Since the problem to be solved by the subject matter of claim 7 is considered to transfect an unspecified decoy into the brain through any other route than direct administration, the subject matter of claim 7 is not characterized in the administration route. So, the subject matter of claim 7 is different from that of claim 1 intended for treating a specific disease called cerebral ischemia using a specific active ingredient called a decoy of NF-κB. Hence, it is not considered that both the subject matters of claims 1 and 7 have a common technical problem not yet solved before the filing date of the present application.

Therefore, the subject matters of claims 7-10 and the subject matters of claims 1-6, respectively of the present application are not considered to be a group of inventions so linked as to form a single general inventive concept.

Document: WO, 99-1155, A1 (Fujisawa Pharmaceutical Co., Ltd.), 14 January, 1999 (14.01.99)

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-10.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-10	NO
Inventive step (IS)	Claims		YES
	Claims	1-10	NO
Industrial applicability (IA)	Claims	1-10	YES
	Claims		NO

2. Citations and explanations

Document 1: "Nuclear Factor-κB Decoy Attenuates Neuronal Damage after Global Brain Ischemia: A Future Strategy for Brain Protection during Circulatory Arrest," (Takayoshi Ueno, et al.), Journal of Thoracic and Cardiovascular Surgery, 2001, Vol. 122, No. 4, pages 720-727
Document 2: EP, 1008352, A1 (Fujisawa Pharmaceutical Co., Ltd.), 14 June, 2000 (14.06.00)
Document 3: EP, 824918, A1 (Fujisawa Pharmaceutical Co., Ltd.), 25 February, 1998 (25.02.98)
Document 4: WO, 96-22112, A1 (Genetic Therapy Inc.), 25 July, 1996 (25.07.96)

Novelty:

Document 1 describes that if a liposome containing a decoy of NF-κB containing sequence GGATTTCCC is administered to a carotid artery, the said gene can be transfected in the brain, thereby inhibiting the neural damage caused by cerebral ischemia (Abstract, Figs. 1-4).

Therefore, the subject matters of claims 1-10 of the present application do not appear to be novel, since they are described in document 1.

Document 2 describes that if a liposome containing a decoy of NF-κB is administered into the brain, encephalopathy such as subarachnoid hemorrhage can be healed (claims 1-4, paragraph [0017], examples).

Therefore, the subject matters of claims 1-4 of the present invention do not appear to be novel, since they are described in document 2.

Document 4 describes a method in which a vector containing a gene is administered into a carotid artery, to transfect cerebrovascular cells (claims 1-6), and also describes that the said vector can also be a liposome preparation (page 14, lines 28-32).

Therefore, the subject matters of claims 7, 8 and 10 of the present application do not appear to be novel, since they are described in document 4.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The following document 5 describes that even if a decoy of NF-κB is administered, the neural cell damage of hippocampus by ischemia cannot be inhibited (page 4672, right column, line 22 to page 4673, left column, line 3, Fig. 5).

Therefore, the subject matters of claims 1-6 of the present application are not sufficiently supported by the specification.

Document 5: "Activation of the Nuclear Factor-κB Is a Key Event in Brain Tolerance," (Nicolas Blondeau, et al.), Journal of Neuroscience, 2001, Vol. 21, No. 13, pages 4668-4677

Claim 6 of the present application describes "a composition used for transfecting a gene in the brain through any other route than direct administration to the brain, characterized by containing at least one decoy and ..."

However, the specification of the present application particularly discloses only that a gene is transfected through the route of a carotid artery during ischemia, and does not describe anything to show that the said transfection can be performed in a state free from ischemia.

Moreover, when the present application was filed, it is considered to have been a matter well-known to a person skilled in the art that (1) since the transition of substances in blood to the brain is selectively allowed by the blood brain barrier, polymeric substances and the like do not easily pass, but (2) only in specific cases such as cerebral ischemia and cerebral tumor, the barrier is destroyed to allow normally impassable substances to pass. Furthermore, when the present application was filed, it is not considered to have been well-known to a person skilled in the art that a decoy generally passes through the blood brain barrier. So, the subject matters of claims 7-10 of the present application are not sufficiently supported by the specification, except those administered to patients having a specific cerebral disease such as ischemia.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : V

Inventive step:

Document 3 describes that a liposome containing a decoy of NF-κB containing sequence GGATTTCCC is used for curing diseases caused by NF-κB (claims 1-4, examples 1-3), and also describes ischemic cerebral diseases as diseases caused by the NF-κB (page 2, lines 35-40).

So, it is considered to be obvious for a person skilled in the art to use the liposome containing the decoy of NF-κB described in document 3 for curing ischemic cerebral diseases.

Therefore, the subject matters of claims 1-5 of the present application do not appear to involve an inventive step.

No special inventive idea is necessary for using the decoy described in document 3 instead of the decoy of NF-κB described in document 2.

Moreover, even if the specification of the present application is read, it is not considered either that any special effect which could not have been predicted by a person skilled in the art from documents 2 and 3 is exhibited because of the specified sequence.

Therefore, the subject matters of claims 1-5 of the present application do not appear to involve an inventive step.